

Human caspase-1 (SEQ ID NO: 1)
 Human caspase-13^a (SEQ ID NO: 2)
 Human caspase-4 (SEQ ID NO: 3)
 Human caspase-5 (SEQ ID NO: 4)
 Human caspase-12 (SEQ ID NO: 4)
 Mouse caspase-12 (SEQ ID NO: 5)
 Mouse caspase-11 (SEQ ID NO: 5)
 conserved amino acids^b

Human caspase-1	(SEQ ID NO: 1)
Human caspase-13 ^a	(SEQ ID NO: 2)
Human caspase-4	(SEQ ID NO: 3)
Human caspase-5	(SEQ ID NO: 4)
Human caspase-12	(SEQ ID NO: 4)
Mouse caspase-12	(SEQ ID NO: 5)
Mouse caspase-11	(SEQ ID NO: 6)
conserved amino acids ^b	

Human caspase-1 (SEQ ID NO: ____)
 Human caspase-13^a (SEQ ID NO: ____)
 Human caspase-4 (SEQ ID NO: ____)
 Human caspase-5 (SEQ ID NO: ____)
 Human caspase-12 (SEQ ID NO: 4)
 Mouse caspase-12 (SEQ ID NO: ____)
 Mouse caspase-11 (SEQ ID NO: ____)
 conserved amino acids^b

Human caspase-1	(SEQ ID NO: ____)
Human caspase-13 ^a	(SEQ ID NO: ____)
Human caspase-4	(SEQ ID NO: ____)
Human caspase-5	(SEQ ID NO: ____)
Human caspase-12	(SEQ ID NO: 4)
Mouse caspase-12	(SEQ ID NO: ____)
Mouse caspase-11	(SEQ ID NO: ____)
conserved amino acids ^b	

MADKVLEKEKRKLFIRSMG
MAEDKHKNPKLMLESLG
MAEGNHRKKPLKVLESLG
MFKGILQSLDNFVNHMLKNNVAGQTSIQTIVPNTDQKSTSVKRDNHKKKTIVMLEYLG
VHMVKLLI
MAARRTHERDPYIKIGLA
MAENKHPDKPLKVLEQLG

EGTINGLIDDELLQOTRVLNKEEMEKVKRENTAVMDKTRALIDSVIPKGQAQCQICITYICE
KELLSIGLDDFVEKVLKLEEEKKKIYDAKLQDKARVLVDISIKNQOEAGQVFVQTFLN
KDFTLTGVLNDLNVEQNVLNWKEEKKKYDAKTEDKVRMADSMQEKORMAQGMQLQTFFN
KDVLHGVFNYLAKHDVLTLKEEKKKYDAKIEDKALILVDSL - KNRVAHOMFTOTLN
KTFLDGGFDLMMENVLNTDEIHIGKCLKFVVSNAAENLVDDITETAQIAKGKFREHLMN
KDMLDGVFDDLVKEVNVLNGDELLKIGESASFILNKAENLVENFLEKTDMAGKIFAGHIAN
KEVLTTEYLEKLVQSNVLKLKEEDQKFNNAERSDKRWVFVDAKKHKSKVGEMLLQTFFS

EDSYLAGTGLSADQ	- - - - - TSGNYLNMODSQGVLLSSFPAPQAQDN	- - - - - PAMPTS
ID	- - - - - KNS	- - - - - PDES V-
ID	- - - - - QIS	- - - - - PPES G-
MD	- - - - - QKI	- - - - - PPESA-
 SKKQLLS		
SQEQLSLQFSNDEDDGPQKICTPSSPSESKRKVEDDEMVNAGLAHESHLMLTAPHGLQS		
VD	- - - - - PGS	- - - - - PEE- HHGEANLEMEE -

FIGURE 1

Human caspase-1 (SEQ ID NO:)
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 Human caspase-4 (SEQ ID NO:)
 Human caspase-5 (SEQ ID NO:)
 Human caspase-12 (SEQ ID NO:)
 Mouse caspase-12 (SEQ ID NO:)
 Mouse caspase-11 (SEQ ID NO:)
 conserved amino acids^b

Human caspase-1	(SEQ ID NO: <u> </u>)
Human caspase-13 ^a	(SEQ ID NO: <u> </u>)
Human caspase-4	(SEQ ID NO: <u> </u>)
Human caspase-5	(SEQ ID NO: <u> </u>)
Human caspase-12	(SEQ ID NO: <u> </u>)
Mouse caspase-12	(SEQ ID NO: <u> </u>)
Mouse caspase-11	(SEQ ID NO: <u> </u>)

conserved amino acids^b

KHSEQVPDILQLNAAIFNMLNTKNCPSLKDCKPVIIQACRGDSPGUVFKDSVG-VSGNL
MHSEEEPDVLVYDTPRTFNNRNCISSLKDCKPVIIIVQACRGANRGELWVSDSPP-ALADS
VHDEKKPDVLVLYDTIFQJ.FNNRNCISSLKDCKPVIIIVQACRGANRGELWVRSSPA-SLEVA
AHKKKKPDVLVLYDTIFQJFNNRNCISSLKDCKPVIIIVQACRGKGEKHKGELWVRSSPA-SLAVI
KHWDQECPDVLDHDDTFFEJFNNRNCISSLKDCKPVIIIMQACRGNGAGIVWFTTDGSKASADT
KHRNKKPDVLHDITFKIJFNNNSCRLRNPKILIMQACRGRYNGTIIVWSTNKGIATADT
MHSEKTPDVLYQDITYIQJFNNCHCPLGRDKPKVIIIVQACRGNSGEMWIRESSK-PQLCR

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 Mouse caspase-12 (SEQ ID NO:)
 Mouse caspase-11 (SEQ ID NO:)
 conserved amino acids^b

SLP - TTEFEDDAIKKAAHIEKODFIACCSSTPDNVSWRHTMGSVFIGRLIEHMQEYACSC
FSQ - SSENLEEDAVYKTHVEKDIFIAFCSSSTPHNVSWRDIKKGSLLFTRLITCFQKYAWCC
SSQ - SSENLEEDAVYKTHVEKDIFIAFCSSSTPHNVSWRDTMGSIFITOLITCFQKYWSWC
SSQ - SSENLEADSVCVKTHEEKDFIAFCSSSTPHNVSWRDRTRGSIIFTTELITCFQKYSSCC
HGRLLQGNICNDAVTKAHVEKDIFIAFKSSTPR-----
DEERVLCKWNNSITYKAHVETDIFIAFKSSTPHNISWKVGKTGSSLFISKLIDCFKKYCWY
GVD - LPRNMEADEVKLISHVEKDIFIAFYSTTIPHLSYRDKTGGSYFTRLISCPRKHACSC
..... * * * * *

Human caspase-1	(SEQ ID NO: ____)
Human caspase-13 ^a	(SEQ ID NO: ____)
Human caspase-4	(SEQ ID NO: ____)
Human caspase-5	(SEQ ID NO: ____)
Human caspase-12	(SEQ ID NO: 4)
Mouse caspase-12	(SEQ ID NO: 4)
Mouse caspase-11	(SEQ ID NO: ____)
conserved amino acids ^b	

DVEE1IFRKVRFQFSEQPDGRAQMPTTERVTLTRCFYLFPGH
 HLEEVFRKVQQSFEEKPNVYKAQMPTVERLSMTRYFYLFPGN
 HLEEVFRKVQQSFETPRAKAQMPTIERLSMTRYFYLFPGN
 HLMEIFRKVQKSFEVYQAKAQMPTIERATLTDFYLFPGN
 -----SHSFETPNILTQOPTIERLSMTRYFYLFPGN
 HLEE1IFRKVQHSFSEVPGELTQMPTIERVSMTRYFYLFPGN
 HLFDFIKVQQSFKEKASIHSMOPTIDRATLTRYFYLFPGN

^a translated amino acid sequence from putative human caspase-13 in EMBL database

"**" means amino acid is identical for all sequences
 ":" means amino acids are considered conservative substitutions among all sequences

FIGURE 2

	1	50
hCaspase-12	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Ap	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Bp	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Cp	MADEKPSXGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Dp	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Ep	-----	
KW-Fp	-----	
KW-Gp	-----	
KW-Hp	-----	
KW-Ip	-----	
KW-Jp	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
KW-Kp	MADEKPSNGV LVHMKVKLLIK TFLDGIFDDL MENNVLNTDE IHLIGKCLKF	
	51	100
hCaspase-12	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSSALLE IQGAQPSGKL	
KW-Ap	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSS.....	
KW-Bp	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSS.....	
KW-Cp	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSS.....	
KW-Dp	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSS.....	
KW-Ep	-----	PSGKL
KW-Fp	-----	AQPSGKL
KW-Gp	-----	AQPSGKL
KW-Hp	-----	AQPSGKL
KW-Ip	-----	AQPSGKL
KW-Jp	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSS.....	
KW-Kp	VVSNAENLVD DITETAQIAG KIFREHLWNS KKQLSSALLE IQGAQPSGKL	
	101	150
hCaspase-12	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Ap IY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Bp IY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Cp IY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Dp IY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Ep	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Fp	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Gp	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Hp	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Ip	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Jp IY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
KW-Kp	KLCPHAHFHE LKT KRADEIY PVMEKERRTC LALNIRNKEF NYLHN RNGSE	
	151	200
hCaspase-12	LDLLGM RDLL ENLGYSVVIK ENLTAQEMET ALRQFAAHPE HQSSDSTFLV	
KW-Ap	LDLLGM * DLL ENLGYSVVIK ENLTAQEMET ALRQFAAHPE HQSSDSTFLV	
KW-Bp	LDLLGM * DLL ENLGYSVVIK ENLTAQEMET ALRQFAAHPE HQSSDSTFLV	
KW-Cp	LDLLGM * DLL ENLGYSVVIK ENLTAQ.....	
KW-Dp	LDLLGM * DLL ENLGYSVVIK ENLTAQ.....	
KW-Ep	LDLLGM * DLL ENLGYSVVIK ENLTA.....	
KW-Fp	LDLLGM * DLL ENLGYSVVIK ESLTAQEMET ALRQFAAHPE HQSSDSTFLV	
KW-Gp	LDLLGM * DLL ENLGYSVVIK ENLTAQ.....	
KW-Hp	LDLLGM * DLL ENLGYSVVIK ENLTAQ.....	
KW-Ip	LDLLGM * DLL ENLGYSVVIK ENLTAQEMET ALRQFAAHPE HQSSDSTFLA	
KW-Jp	LDLLGM * DLL ENLGYSVVIK ENLTAQEME..... STFLV	
KW-Kp	LDLLGM * DLL ENLGYSVVIK ENLTAQEMET ALRQFAAHPE HQSSDSTFLV	

	201	250
hCaspase-12	FMSHGILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
KW-Ap	FMSHSILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
KW-Bp	FMSHSILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
KW-Cp
KW-Dp
KW-EpSILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
KW-Fp	FMSHSILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
KW-Gp
KW-Hp
KW-Ip	FMSHSILNRI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPK.....	
KW-Jp	FMSHSILNGI CGTKH-----	-----
KW-Kp	FMSHSILNGI CGTKHWDQEP DVLHDDTIFE IFNNRNCQL KDKPKVIIMQ	
	251	300
hCaspase-12	ACRGNGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-Ap	ACRGNGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-Bp	ACRGNGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-CpGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-DpGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-Ep	ACRG-----	-----
KW-Fp	AC-----	-----
KW-GpGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-HpGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
KW-IpGAGIV WFTTDVEKAS ADTHGRLLQG NICNDAVTKV HVEKDFIAFK	
KW-Jp	-----	-----
KW-Kp	ACRGNGAGIV WFTTDSGKAS ADTHGRLLQG NICNDAVTKA HVEKDFIAFK	
	301	350
hCaspase-12	SSTPHNVSWR HETNGSVFIS QIIYYFREYS WSHHLEEIFQ KVQHSFETPN	
KW-Ap	SSTPHNVSWR HETNGSVFIS QIIYYFREYS WSHHLEEIFQ KVQHSFETPN	
KW-Bp	SSTP.....VQHSFETPN
KW-Cp	SSTPHNVSWR HETNGSVFIS QIIYYFREYS WSHHLEEIFQ KVQHSFETPN	
KW-Dp	SSTP.....VQHSFETPN
KW-Ep	-----	-----
KW-Fp	-----	-----
KW-Gp	SSTP.....VQHSFETPN
KW-Hp	SSTPHNVSWR HETNGSVFIS QIIYYFREYS WSHHLEEIFQ KVQHSFETPN	
KW-Ip	SSTP.....VQHSFETPN
KW-Jp	-----	-----
KW-Kp	SSTPHNVSWR HETNGSVFIS QIIYYFREYS WSHHLEEIFQ KVQHSFETPN	
	351	374
hCaspase-12	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Ap	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Bp	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Cp	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Dp	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Ep	-----	-----
KW-Fp	-----	-----
KW-Gp	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Hp	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Ip	ILTQLPTIER LSMTRYFYLF PGN*	
KW-Jp	-----	-----
KW-Kp	ILTQLPTIER LSMTRYFYLF PGN*	

L_a aln

Human Caspase-12 compared to Mouse Caspase-12 with CARD domain, ICE-p20 domain, ICE-p10 domain and Active-site amino acids described.

Legend for Domains as calculated by PFAM

CARD Domain	xxxxxxxx
ICE-p20 Domain	yyyyyyyy
ICE-p10 Domain	zzzzzzzz

Active-Site Residues: H...C

Calpain and Auto-catalytic cleavage sites determined for Mouse Caspase-12

FIGURE 3

H12_a_~1

CLUSTAL W (1.7) multiple sequence alignment

h_Caspase-3 -----
h_Caspase-7 -----
h_Caspase-12 -----MADE
m_Caspase-12 -----MAAR
h_Caspase-4 -----MAEG
h_Caspase-13 -----MAED
h_Caspase-5 -----MFKGILQSGLDNFVINHMLKNNVAGQTSIQLTVPNTDQKSTSVKKD
h_Caspase-1 -----MAD
h_Caspase-6 -----
h_Caspase-8 -----MDFSRNLYDIGEQLDSEDLASLKFLSLDYIPQRKQEPIKDALM
h_Caspase-10 -----MKSQGQHWYSSSDKNCKVSFREKLLIIDSNLGVQDVENLKFCLIGLVPNKKLEKSSSASD
h_Caspase-9 -----MDE
h_Caspase-2 -----MAADRGRRIILGVCGM
h_Caspase-14 -----

h_Caspase-3 -----
h_Caspase-7 -----
h_Caspase-12 -----KPSNGVLVHMVK---LLIKTFLDGI--FDDLMENNVLNTDEIHLIKCL-KFVVSN
m_Caspase-12 RTHERDPIYKIK---GLAKDMFLDGV--FDDLVKEVNLNGDELLKIGESA-SFILNKA
h_Caspase-4 N-HRKKPLKVLE---SLGKDFLTGV--LDNLVEQNVLNWKEEEKKYYD-AKTEDKVR
h_Caspase-13 K-HNKNPLKMLE---SLGKELISGL--LDDFVEKVNVLKLEEEKKKIYD-AKLQDKAR
h_Caspase-5 N-HKKKTVKMLE---YLGKDVHGV--FNYLAKHDVTLKLEEEKKYYD-AKIEDKAL
h_Caspase-1 I-KVLKEKRKLFIR---SMGETTINGL--LDELLQTRVLNKEEMEKVKREN-ATVMDKTRA
h_Caspase-6 -----
h_Caspase-8 -----LFQRLQEKRMLLEESNLSFLKELLFRINRLDLLITYLNTRKEEMEREQTPGRAQISAYRV
h_Caspase-10 VFEHLLAEDLLSEEDPFFLAELLYIIR-QKLLLQHLNCTKEEVERLLPTR--QRVSLFRN
h_Caspase-9 ADRRLLLRRCRLR---LVEELQVDQLWDALLSELFRPHMIEDIQRAGSGSRRDQARQ
h_Caspase-2 HPHHQETLKKNR---VVLAKQLLSELLEHLLEKDIITLEMRELIQAKV--GSFSQNVE
h_Caspase-14 -----

h_Caspase-3 -----MENTEN--SVDSK-SIKNLEPKIIH---GSE-----
h_Caspase-7 -----MADDQGCIEEQGVVEDSANED--SVDAKPDRSSFVPSLFS---KKKKN-----
h_Caspase-12 LVDDITETAQIAGKIFREHLWNS---KKQLSSALL-EIQGAQ---PSG---K---
m_Caspase-12 LVENFLEKTDMAGKIFAGHIANS---QEQLSLQFSNDEDGPQKICTPSSPSESKRKV
h_Caspase-4 MADSMQEKRQRMAGQMQLLQTFFNID---QISPNNKAHPNMEAGPP---ESGES-----
h_Caspase-13 LVDSIRQKNQEAGQVFVQTFLNID---KNSTSIAPEETVAGPD---ESVGS-----
h_Caspase-5 LVDSL-R-KNRVAHQMFQTLLNMD---QKITSVKPLLQIEAGPP---ESAES-----
h_Caspase-1 LIDSVIPKGAAQACQICITYICEEDS--YLAGTLGLSADQTSGNYLNMQDSQGVLS
h_Caspase-6 SFPA-----MSSASGLRRGHYPAGGE---EN-----
h_Caspase-8 MLYQISEEVRSSELRSFKFLQQEEISKCKLDDDMNLLDIFIEMEKR
h_Caspase-10 VILGEKGKLDILKRV
h_Caspase-9 LLYELSEGIDSENLKDMIFLLKDSLP-KTEMTSLSFLAFLEKQGK--IDE
h_Caspase-2 DNLTCLEDL
h_Caspase-14 LIIDLETRGSQALPLFISCLEDTG---QDMLASFLRTNRQA
h_Caspase-14 AKLSKPTLENLTPV
h_Caspase-14 VLRP
h_Caspase-14 LLNLLPKRGPA
h_Caspase-14 QAFDAFCEALRET
h_Caspase-14 KQGHLEDMLL
h_Caspase-14 TTSGLQHV
h_Caspase-14 LPP
h_Caspase-14 SCDY
h_Caspase-14 DLS
h_Caspase-14 LPFP
h_Caspase-14 VCE

FIGURE 4

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_h_Caspase-3 -----SMDSS--GISLDN-----
_h_Caspase-7 -----VTMRS--IKTTRDRVPTY-
_h_Caspase-12 -----LKLCPHAHFHELTKRADE-
_m_Caspase-12 EDDEMEVNAGLAHES--HLM---LTAPHGLQSSEVQDTLKCPRDQFCKIKTERAKE-
_h_Caspase-4 -----TDALKLCPHEEFLRLCKERAEE-
_h_Caspase-13 -----AATLKLCPHEEFLKLCKERAGE-
_h_Caspase-5 -----TNILKLCPREEFLRLCKKNHDE-
_h_Caspase-1 PQA VQD-----NPAMPTSSGSEG NVKLC SLEEAQR IW KQK SAE-
_h_Caspase-6 -----MTETDAFYKREMFDPAE-
_h_Caspase-8 CAQINKSLLKIINDY--EEFSKERSSSLEGPSPDEFNSGEELCGVMTISDSPREQDSE-
_h_Caspase-10 CKTVVPKLLRNIEKYKREKAIQIVTPPV DKEAES YQGEEELVSQTDVKTFL EALP QESWQ
_h_Caspase-9 EIRK-----PEVLRPETPRPV DIGSGGF GDVG ALES LRG NAD-
_h_Caspase-2 SCPL YKKLR-----LSTD TVEHSLDN KDG PVL QVKP CTPEF YQTH FQ-
_h_Caspase-14 -----

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h_Caspase-3	-----	SYKMDYPEMGLCIIINNKN
h_Caspase-7	-----	QYNMNFEKLGKCIINNKN
h_Caspase-12	-----	IYPVMEKERRTCLALNIRN
m_Caspase-12	-----	IYPVMEKEGRTRLALIICN
h_Caspase-4	-----	IYPIKERNNRTRLALIICN
h_Caspase-13	-----	IYPIKERKDTRLALIICN
h_Caspase-5	-----	IYPIKKREDRRRLALIICN
h_Caspase-1	-----	IYPIIMDKSSRTRLALIICN
h_Caspase-6	-----	KYKMDHRRRGIALIFNHER
h_Caspase-8	-----	SQTLDKVYQMKS KPRGYCLIINHN
h_Caspase-10	NKHAGSNGNRATNGAPS LVS RGM QGASANTLNSETSTKRAAVYRMNRNH RGLCVIVNNHS	
h_Caspase-9	-----	LAYILSMEPCGHCLIINNVN
h_Caspase-2	-----	LAYRLQSRP RGLALVLSNVH
h_Caspase-14	-----	MSNPRSLEEEKYDMMSGARLA

<i>h_Caspase-3</i>	FH-----KSTGMTSRSGTDVDAANLRETFRNLKYEVRNK-NDLTREIEVELMRDVSKE
<i>h_Caspase-7</i>	FD-----KVTGGMGVNRNGTDKDAEALFKCFRSLGF DVIVY- NDCSCAKMQDLLKKASEE
<i>h_Caspase-12</i>	K-----EFNYLHNRRNGSELDLLGMRDLLENLGYSVVIKENLTAQEMETALRQFAAHP
<i>m_Caspase-12</i>	K-----KFDYLFDRDNADTDILNMQELLENLGYSVVLKENLTAQEMETELMQFAGRP
<i>h_Caspase-4</i>	T-----EFDHLPPRNGADFDTGMKELLEG LDYSVDVEENLTARDMESALRAFAATRP
<i>h_Caspase-13</i>	T-----EFDHMPPRNGAALDILGMKQOLLEG LGYTVEVEEKL TARDMESVLUWKFAARE
<i>h_Caspase-5</i>	T-----KFDHLPARNGAHYDIVGMKRLLQGLGYTVVDEKNLTARDMESVLR AFAARP
<i>h_Caspase-1</i>	E-----EFDSIPRRTGAEV DITGMTMLLQNLGY SVDVKKNLTASDMTTELEAF AHRP
<i>h_Caspase-6</i>	FF-----WHLTLPEERRTCADRDNLTRRFSDLGFEV KCFNDLKAEELL LKIHEVSTVS
<i>h_Caspase-8</i>	FAKAREKVPKLHSIRDRNGTHLDAGALTTFEELHFEIKPH-DDCTVEQIYEILK IYQLM
<i>h_Caspase-10</i>	F-----TSLKDRQGTHKDAEILSHVFQWLGF TVIHNNVTKVEMEMVLQKQKCNP
<i>h_Caspase-9</i>	FCR-----E-SGLRTRTGSNIDCEKLRRRFSSPHFMVEVKGDLTAKKMVLALLELAQD
<i>h_Caspase-2</i>	FTG-----EKELEFRSGGDVDHSTLVTLFKLLGYDVHVLCDQTAQEMQEKLQNF AQLP
<i>h_Caspase-14</i>	L-----ILCVTKAREGSEEDLDALEHMFRQLRFESTMKRDP TAEQFQEELEKFQQAI

↓
 h_Caspase-3 D--HSKRSSFVCVLLSHGEEG-----IIFGTNG-----PVDLKKITNFFRGDRCRSL
 h_Caspase-7 D--HTNAACFACILLSHGEEN-----VIYGKD-----VTPIKDLTAHFRGDRCKTL
 h_Caspase-12 E--HQSSDSTFLVFM**H**GILN-----GICGTKHWDQEPDVLHDDTIFEIFNNRNQSL
 m_Caspase-12 E--HQSSDSTFLVFM**H**GILE-----GICGVKHRNKKPDVLHDDTIFKIFNNRNCRSL
 h_Caspase-4 E--HKSSDSTFLVLM**H**GILE-----GICGTVHDEKKPDVLLYDTIFQIFNNRNCLSL
 h_Caspase-13 E--HKSSDSTFLVFM**H**GILD-----GICGTMHSEEPDVLPYDTIFRTFNNRNCLSL
 h_Caspase-5 E--HKSSDSTFLVLM**H**GILE-----GICGTAHKKKKPDVLLYDTIFQIFNNRNCLSL
 h_Caspase-1 E--HKTSDSTFLVFM**H**GIRE-----GICGKHSEQVPDILQLNAIFNMLNTKNCPNL
 h_Caspase-6 --HADADCFVCVFLSHGEGN-----HIYAYDA-----KIEIQTLTGLFKGDKCHSL
 h_Caspase-8 D--HSNMDCFICCI**L**SHGDKG-----IIYGTDG-----QEAPIYELTSQFTGLKCPNL
 h_Caspase-10 A--HADGDCFVFCILT**H**GRFG-----AVYSSDE-----ALIPIREIMSHFTALQCPL
 h_Caspase-9 ---HGALDCCVVVILSHG**C**QASHLQFPGAVYGTDG-----CPVSVEKIVNIFNGTSCPPL
 h_Caspase-2 A--HRVTDSCIVALLSHGVEG-----AIYGVDG-----KLQLQEVFQLFDNANCPL
 h_Caspase-14 DSREDPVS**C**AFVVLMAHGREG-----FLKGEDG-----EMVKLENLFEALNNNKNCQAL

: : ** : : : * * *

↓
 h_Caspase-3 TGKPKLFII IQACRGT--ELDCGIETDSG-----VDDDMAC-----HKIP
 h_Caspase-7 LEKPKLFFI IQACRGT--ELDDGIQADSG-----PINDDANPR-----YKIP
 h_Caspase-12 KDKPKVIIMQACRGN--GAGIVWFTTD-----SGKASADTHG-RLLQGNIC--NDAVTKA
 m_Caspase-12 RNKPKILIMQACRGR--YNGTIWVSTN-----KGIATADTDEERVLS--CKWNNSITKA
 h_Caspase-4 KDKPKVIIVQACRGA--NRGELWVRDSP-----ASLEVASSQSSENLE----EDAVYKT
 h_Caspase-13 KDKPKVIIVQACRGA--NRGELWVSDSP-----PALADSFSQSSENLE----EDAVYKT
 h_Caspase-5 KDKPKVIIVQACRGE--KHGELWVRDSP-----ASLAVISSQSSENLE----ADSVCKI
 h_Caspase-1 h_Caspase-6 KDKPKVII IQACRGD--SPGVVWFKDSV-----GVSGNLSLPTTEEFE----DDAIKKA
 h_Caspase-8 VGKPKIFI IQACRGN--QHDVPIPLDV-----VDNQTEKLDTNITEVD----AASVYTL
 h_Caspase-10 AGKPKVFFI IQACQGDNYQKGIPVETDS-----EEQPYLEMDLS-----SPQTRYI
 h_Caspase-9 AEKPKLFII IQACQGEEIQPSVSIEADALN-----PEQAPTSQ-----DSI
 h_Caspase-2 GGKPKLFII IQACGGEQKDHFEVASTSPEDESPGSNPEPDATPFQEGLRTFDQLDAISSL
 h_Caspase-14 QNKPKMFFI IQACRGDETDRGVDQDGKN-----HAGSPGCEESDAGKE----KLPKMRL
 RAKPKVYYII IQACRGEQRDPGETVGGDE-----IVMVIKDSP-----QTI

***: : : *** * .

h_Caspase-3 VDA-DFLYAYSTAPGYYSWRNSKDGSWFIQSLCAMLKQYA-DKLEFMHILTRVNRKVATE
 h_Caspase-7 VEA-DFLFAYSTVPGYYYSWRSPGRGSWFVQALCSILEEHG-KDLEIMQILTRVNDRVARH
 h_Caspase-12 HVEKDFIAFKSSTPHNVSWRHETNGSVFISQIIYYFREYS-WSHHLEE**I**FQ---KVQHS
 m_Caspase-12 HVETDFIAFKSSTPHNISWKVGKTGSLFISKLIDCFKKYC-WCYHLEE**I**FR---KVQHS
 h_Caspase-4 HVEKDFIAFCSSTPHNWSRDSTMGSIFTQLITCFQKYS-WCCHLEEVFR---KVQQS
 h_Caspase-13 HVEKDFIAFCSSTPHNWSRDTRGSIFTTELITCFQKYS-WCCHLEEVFR---KVQQS
 h_Caspase-5 HEKDFIAFCSSTPHNWSRDTRGSIFTTELITCFQKYS-CCCHLME**I**FR---KVQKS
 h_Caspase-1 HIEKDFIAFCSSTPDNVSRHPTMGSVFIGRLIEHMQEYA-CSCDVEE**I**FR---KVRFS
 h_Caspase-6 PAGADFLMCYSVAEGYYSHRETVNGSWYIQDLCEMPLGKYG-SSLEFTELLTLVNRKVSQR
 h_Caspase-8 PDEADFLGMATVNNCVSYRNPAEGTWYIQSLCQSLRERCPRGDDILTILT---EVNYE
 h_Caspase-10 PAEADFLGLATVPGYVSFRHVEEGSWYIQSLCNHLKKLVPRLKFLEKTM---EIRGR
 h_Caspase-9 PTPSDIFVSYSTFPGFVSWRDPKSGSWYVETLDDIFEQWA-HSEDLQSLLL---RVANA
 h_Caspase-2 PTRSDMICGYACL**K**GTAAMRNTKRGSWYIEALAQVF SERA-CDMHVADM**L**VKN-ALIKD
 h_Caspase-14 PTYTDALHVYSTVEGYIAYRHDQKGSCFIQTLVDVFTKRK---GHILELLT---EVTRR

* : : : : * : : : : : : .. .

<i>h_Caspase-3</i>	FESFSFDATFHAKKQIPCIVSMLTKE--LYFYH---
<i>h_Caspase-7</i>	FESQSDDPHFHEKKQIPCIVSMLTKE--LYFSQ---
<i>h_Caspase-12</i>	FET ---PNILTQLPTIERLSMTRYF--YLFPGN---
<i>m_Caspase-12</i>	FEV----PGELTQMPTIERVSMLTRYF--YLFPGN---
<i>h_Caspase-4</i>	FET----PRAKAQMPTIERLSMTRYF--YLFPGN---
<i>h_Caspase-13</i>	FEK----PNVKAQMPTVERLSMTRYF--YLFPGN---
<i>h_Caspase-5</i>	FEV----PQAKAQMPTIERATLTRDF--YLFPGN---
<i>h_Caspase-1</i>	FEQ----PDGRAQMPTTERVTLTRCF--YLFGH---
<i>h_Caspase-6</i>	RVDFCKDPSAIGKKQVPCFASMLTKK--LHFFPKSN-
<i>h_Caspase-8</i>	VSN--KDDKKNMGKOMPQPTFTLRKK--LVFPSD---
<i>h_Caspase-10</i>	KRTVWG-AKQISATSLPTAISAQTPRPPMRRWSSVS-
<i>h_Caspase-9</i>	VSV-----KGIYKQMPGCFNFLRKK--LFFKTS---
<i>h_Caspase-2</i>	REGYAPGTEFHRCKEMSEYCSTLCRH-LYLFPGHPPPT
<i>h_Caspase-14</i>	MAEAEELVQEGKARKTNPEIQSTLRKR--LYLQ----

Legend:

- ↓ Active-site Residues
- * Identical Residues
- : Conservative Substitution
- . Allowable Substitution

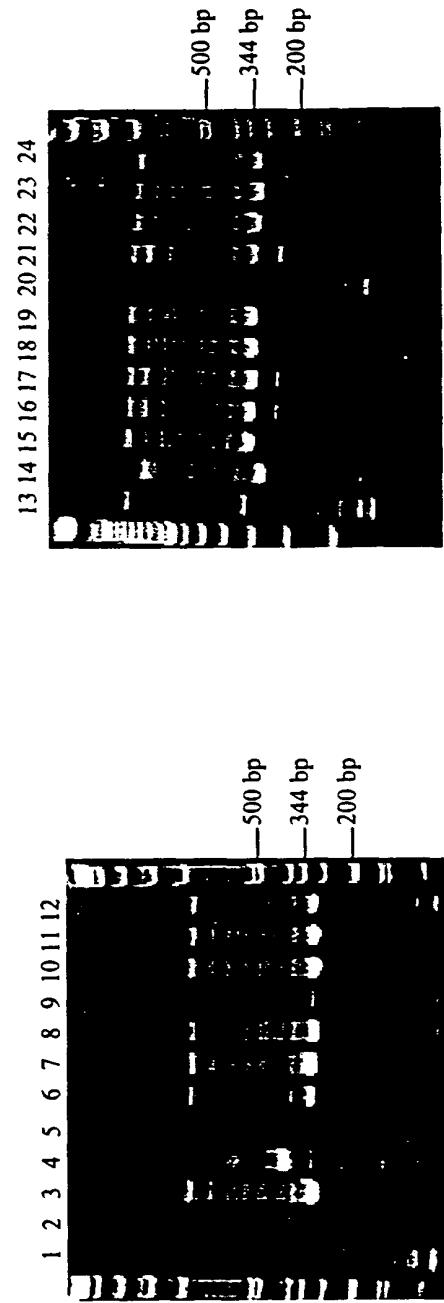
H12_b_~1

CLUSTAL W (1.7) multiple sequence alignment

CARD domain ICE-P20 Domain ICE-P10 Domain Active-site Residues

卷之三

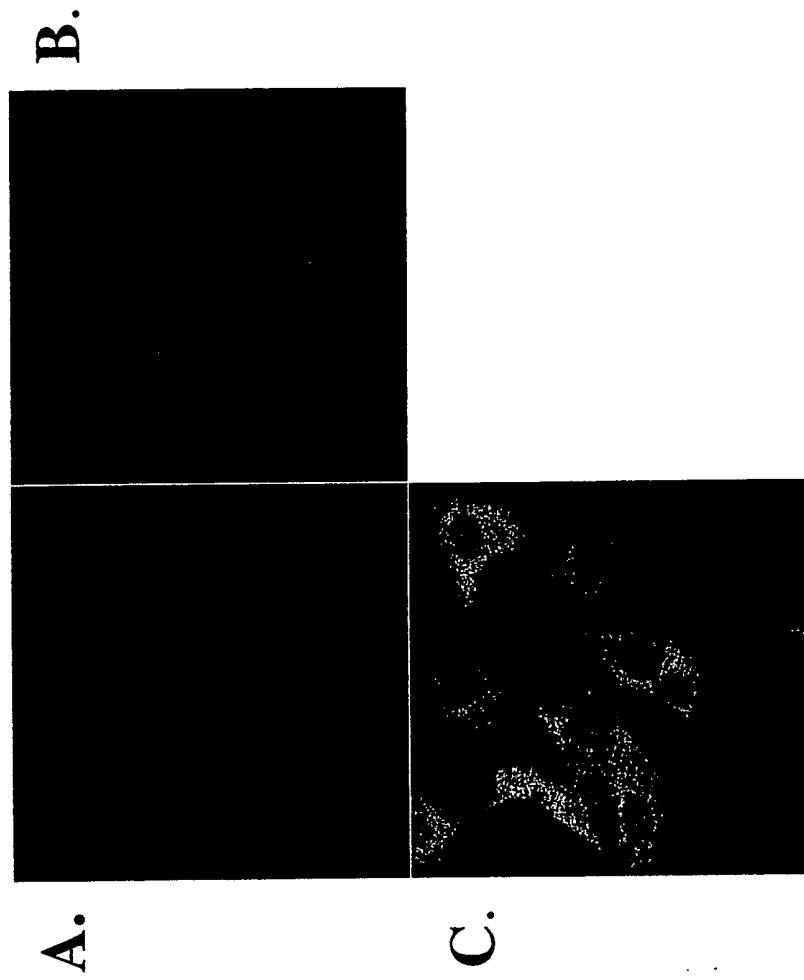
Tissue Profiling of hCaspase-12



1. Brain
2. Heart
3. Kidney
4. Spleen
5. Liver
6. Colon
7. Lung
8. Small Intestine
9. Muscle
10. Stomach
11. Testis
12. Placenta
13. Pituitary
14. Thyroid gland
15. Adrenal gland
16. Pancreas
17. Ovary
18. Uterus
19. Prostate
20. PBL
21. Fetal brain
22. Fetal liver
23. Fat
24. Mammary gland

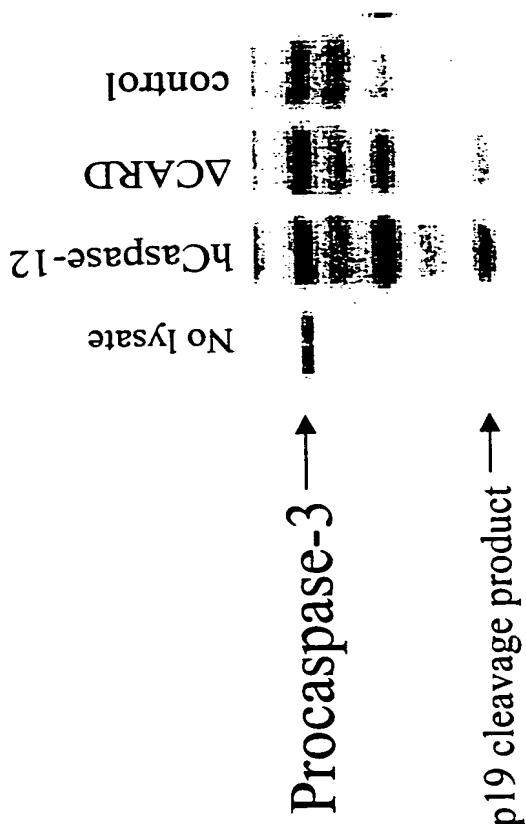
FIGURE 6

FIGURE 7



Cleavage of Procaspace-3 by hCaspace-12

A.



B.

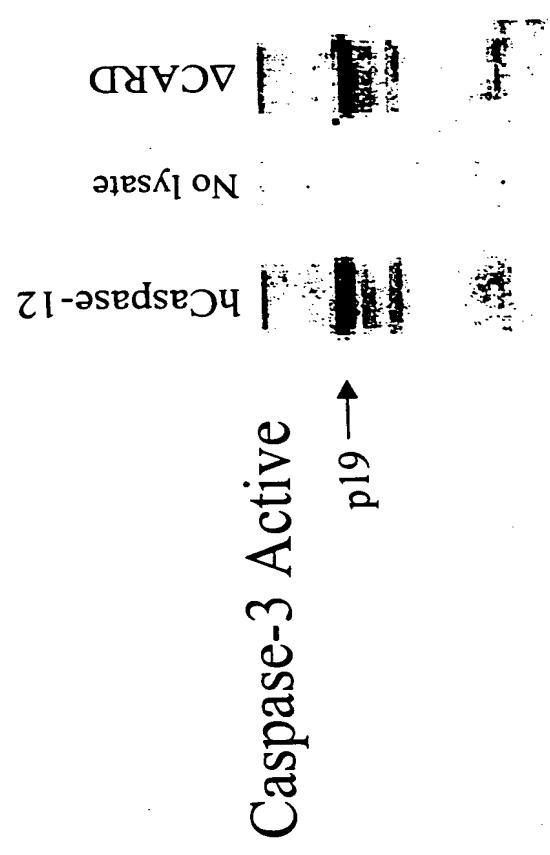
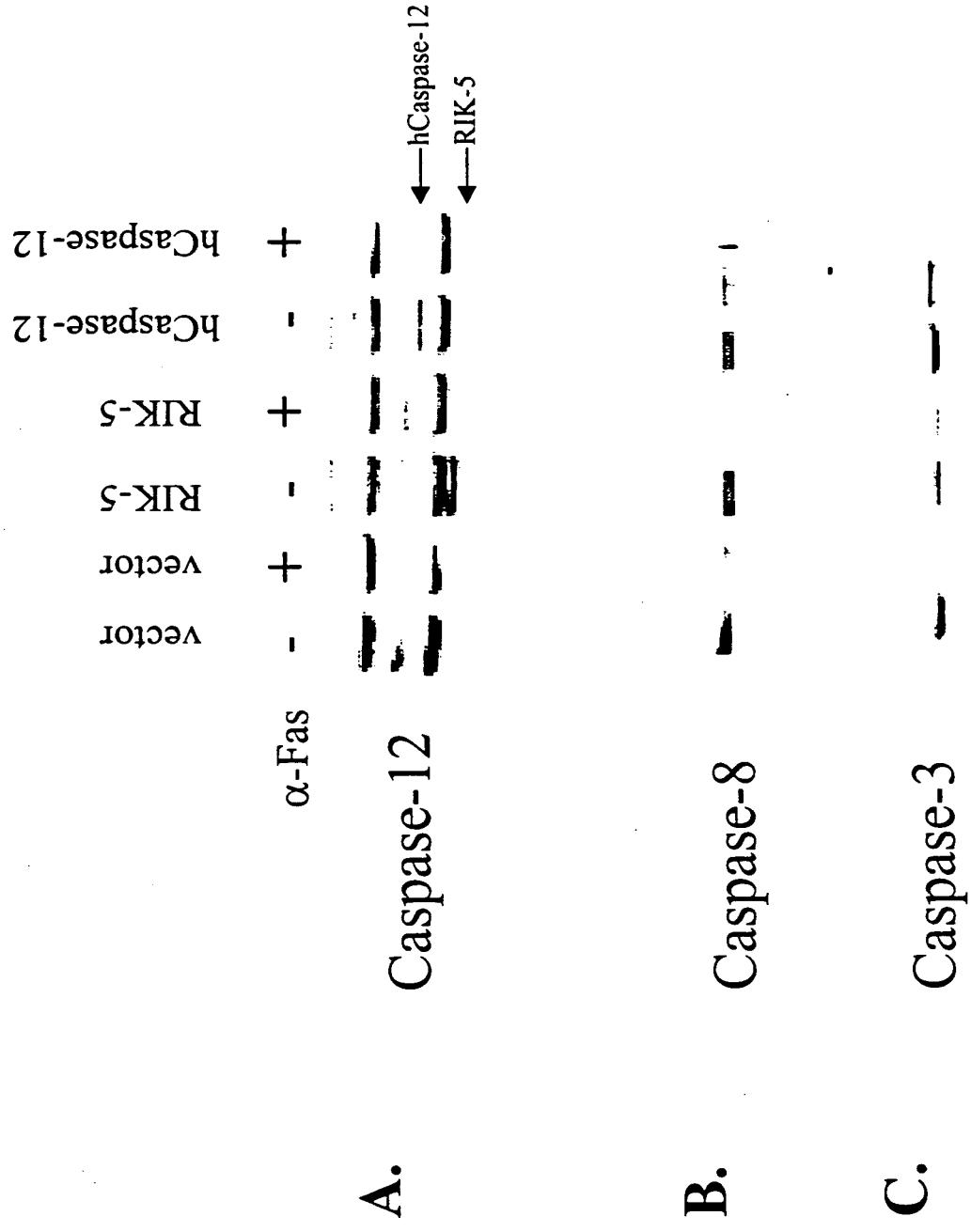


FIGURE 8

SH-EP cell transfection +/- α-Fas

α-Fas - + - + - +
RIK-5
Vector
Vector
Caspase-12
hCaspase-12
hCaspase-12
RIK-5
Vector
α-Fas



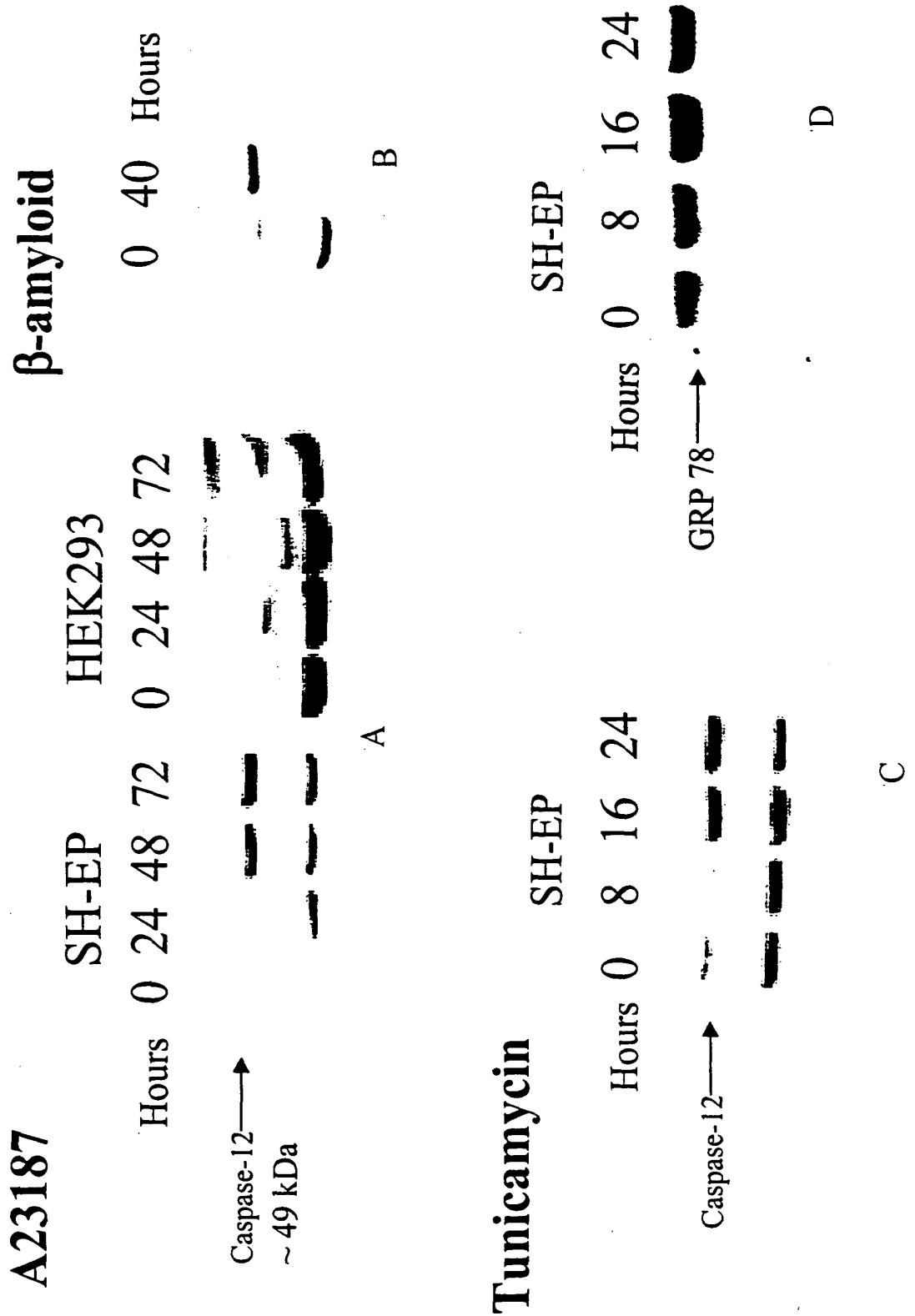


FIGURE 10

FIGURE 11

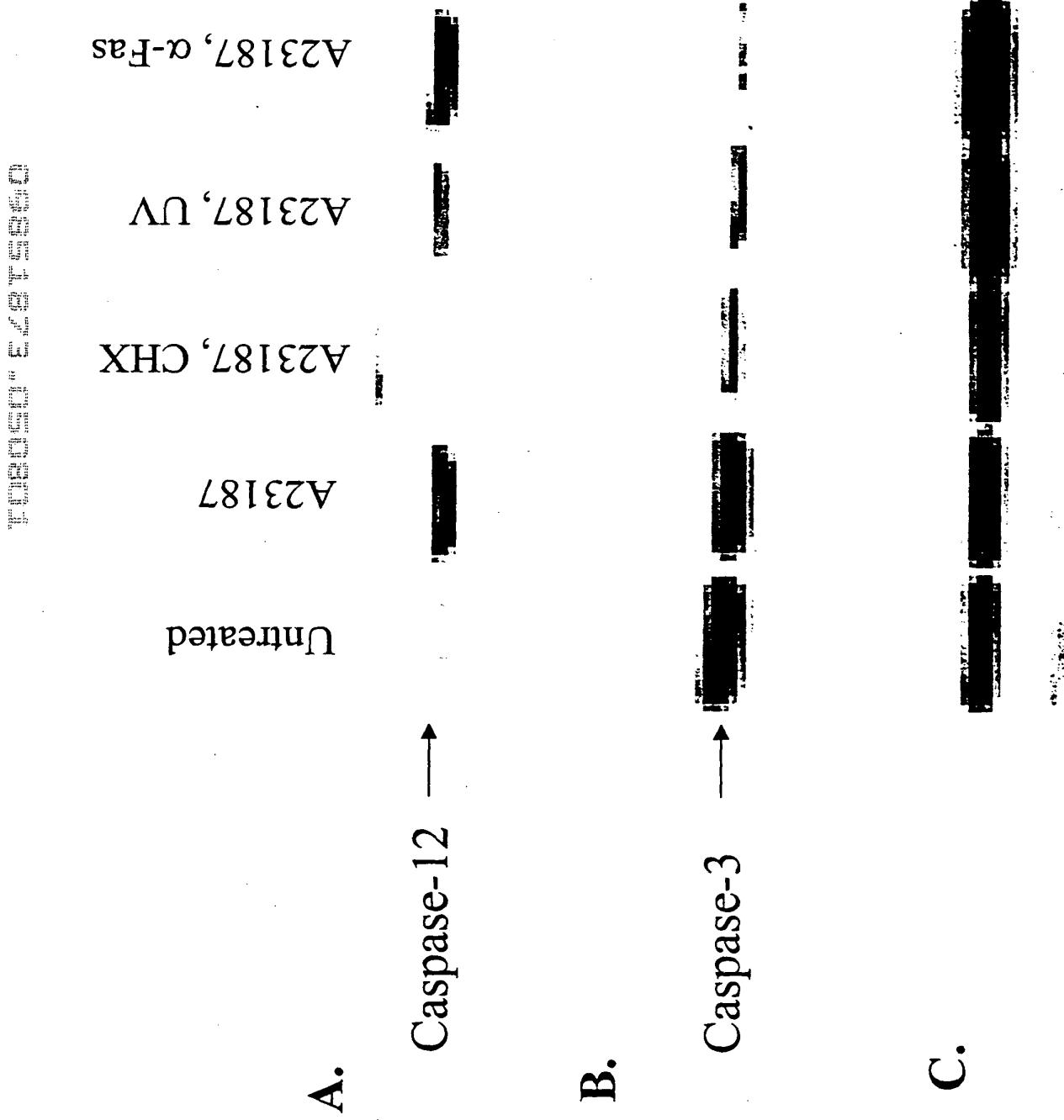


FIGURE 12

SH-EP cells treated with A23187, UV +/- inhibitors

A.

1. 2. 3. 4.

Caspase-12 — — — —

B.

Caspase-3 — — — —

Calpain cleavage of recombinant caspase-12

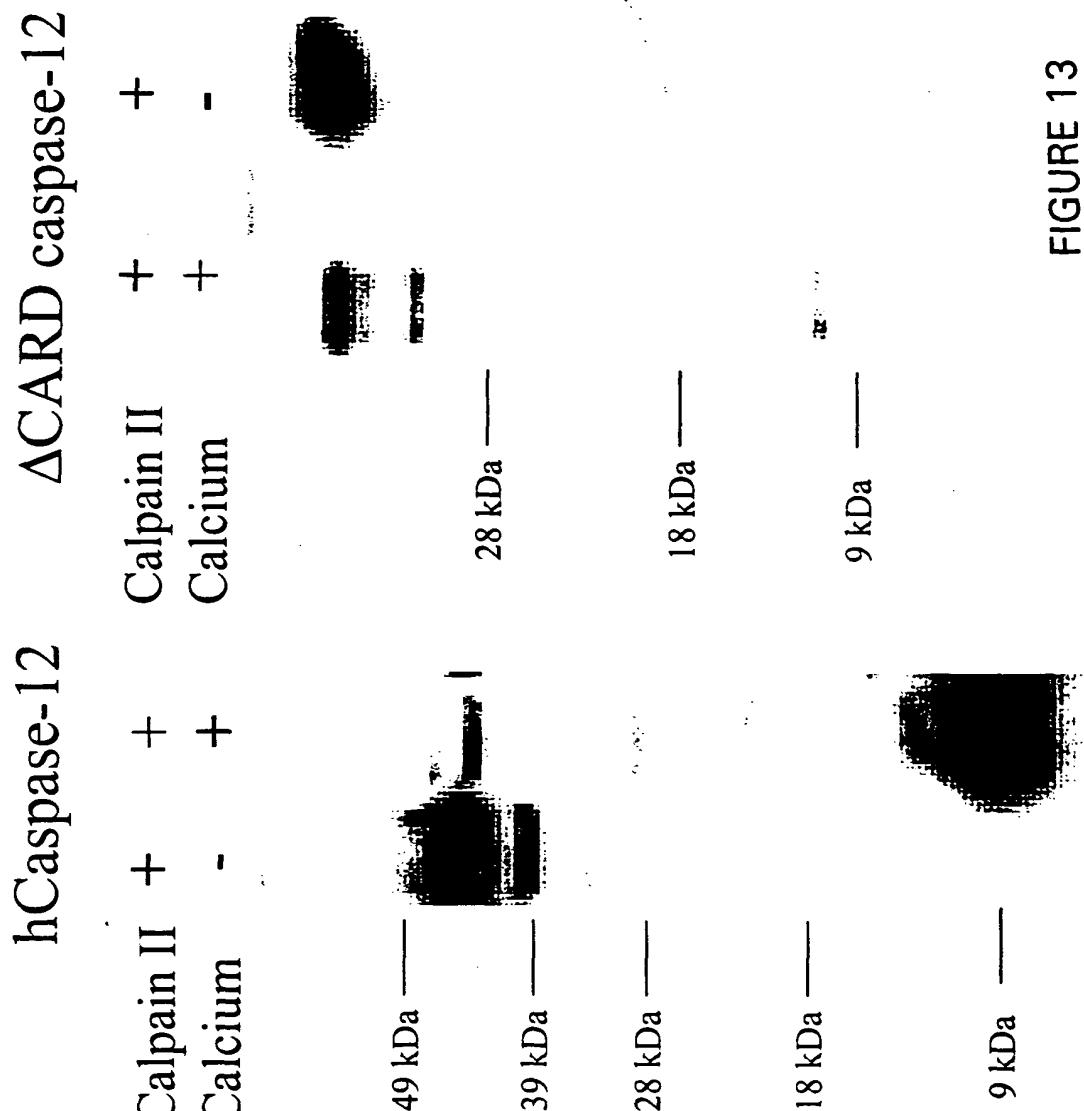


FIGURE 13